#4

SEQUENCE LISTING

<210> Wands, Jack R.
de la Monte, Suzanne M.
Ince, Nedim
Carlson, Rolf I.

<120> DIAGNOSIS AND TREATMENT OF MALIGNANT NEOPLASMS

<130> 21486-032 DIV5

<140> 09/903,248
<141> 2001-07-11

<150> 09/436,184
<151> 1999-11-08

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<170> PatentIn Ver. 2.1

<210> 1
<211> 36
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Consensus
EGF-like domain

<220>
<221> VARIANT
<222> (2)..(8)
<223> Wherein Xaa is any amino acid

<220>
<221> VARIANT
<222> (10)..(13)
<223> Wherein Xaa is any amino acid.

<220>
<221> VARIANT
<222> (15)..(24)
<223> Wherein Xaa is any amino acid.

<220>
<221> VARIANT
<222> (26)

<223> Wherein Xaa is any amino acid.

<220>
<221> VARIANT
<222> (28)..(35)
<223> Wherein Xaa is any amino acid.

<400> 1
Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Cys Xaa Xaa
1   5   10   15

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Cys Xaa Xaa Xaa Xaa Xaa
            20   25   30

Xaa Xaa Xaa Cys
        35

<210> 2
<211> 758
<212> PRT
<213> Homo sapiens

<400> 2
Met Ala Gln Arg Lys Asn Ala Lys Ser Ser Gly Asn Ser Ser Ser Ser
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Gly Ser Gly Ser Gly Ser Thr Ser Ala Gly Ser Ser Ser Pro Gly Ala
            20   25   30

Arg Arg Glu Thr Lys His Gly Gly His Lys Asn Gly Arg Lys Gly Gly
            35   40   45

Leu Ser Gly Thr Ser Phe Phe Thr Trp Phe Met Val Ile Ala Leu Leu
        50   55   60

Gly Val Trp Thr Ser Val Ala Val Val Trp Phe Asp Leu Val Asp Tyr
65   70   75   80

Glu Glu Val Leu Gly Lys Leu Gly Ile Tyr Asp Ala Asp Gly Asp Gly
                85   90   95

Asp Phe Asp Val Asp Asp Ala Lys Val Leu Leu Gly Leu Lys Glu Arg
            100   105   110

Ser Thr Ser Glu Pro Ala Val Pro Pro Glu Glu Ala Glu Pro His Thr
        115   120   125

2

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Glu Pro Glu Glu Gln Val Pro Val Glu Ala Glu Pro Gln Asn Ile Glu
    130                 135                 140

Asp Glu Ala Lys Glu Gln Ile Gln Ser Leu Leu His Glu Met Val His
145                 150                 155                 160

Ala Glu His Val Glu Gly Glu Asp Leu Gln Gln Glu Asp Gly Pro Thr
                165                 170                 175

Gly Glu Pro Gln Gln Glu Asp Asp Glu Phe Leu Met Ala Thr Asp Val
                180                 185                 190

Asp Asp Arg Phe Glu Thr Leu Glu Pro Glu Val Ser His Glu Glu Thr
                195                 200                 205

Glu His Ser Tyr His Val Glu Glu Thr Val Ser Gln Asp Cys Asn Gln
    210                 215                 220

Asp Met Glu Glu Met Met Ser Glu Gln Glu Asn Pro Asp Ser Ser Glu
225                 230                 235                 240

Pro Val Val Glu Asp Glu Arg Leu His His Asp Thr Asp Asp Val Thr
                245                 250                 255

Tyr Gln Val Tyr Glu Glu Gln Ala Val Tyr Glu Pro Leu Glu Asn Glu
                260                 265                 270

Gly Ile Glu Ile Thr Glu Val Thr Ala Pro Pro Glu Asp Asn Pro Val
    275                 280                 285

Glu Asp Ser Gln Val Ile Val Glu Glu Val Ser Ile Phe Pro Val Glu
    290                 295                 300

Glu Gln Gln Glu Val Pro Pro Glu Thr Asn Arg Lys Thr Asp Asp Pro
305                 310                 315                 320

Glu Gln Lys Ala Lys Val Lys Lys Lys Pro Lys Leu Leu Asn Lys
                325                 330                 335

Phe Asp Lys Thr Ile Lys Ala Glu Leu Asp Ala Ala Glu Lys Leu Arg
                340                 345                 350

Lys Arg Gly Lys Ile Glu Glu Ala Val Asn Ala Phe Lys Glu Leu Val
    355                 360                 365

Arg Lys Tyr Pro Gln Ser Pro Arg Ala Arg Tyr Gly Lys Ala Gln Cys
    370                 375                 380
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3

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Glu Asp Asp Leu Ala Glu Lys Arg Arg Ser Asn Glu Val Leu Arg Gly
385                 390             395                 400

Ala Ile Glu Thr Tyr Gln Glu Val Ala Ser Leu Pro Asp Val Pro Ala
                405             410                 415

Asp Leu Leu Lys Leu Ser Leu Lys Arg Arg Ser Asp Arg Gln Gln Phe
            420             425             430

Leu Gly His Met Arg Gly Ser Leu Leu Thr Leu Gln Arg Leu Val Gln
            435             440             445

Leu Phe Pro Asn Asp Thr Ser Leu Lys Asn Asp Leu Gly Val Gly Tyr
        450             455             460

Leu Leu Ile Gly Asp Asn Asp Asn Ala Lys Lys Val Tyr Glu Glu Val
465                 470             475                 480

Leu Ser Val Thr Pro Asn Asp Gly Phe Ala Lys Val His Tyr Gly Phe
            485             490             495

Ile Leu Lys Ala Gln Asn Lys Ile Ala Glu Ser Ile Pro Tyr Leu Lys
            500             505             510

Glu Gly Ile Glu Ser Gly Asp Pro Gly Thr Asp Asp Gly Arg Phe Tyr
        515             520             525

Phe His Leu Gly Asp Ala Met Gln Arg Val Gly Asn Lys Glu Ala Tyr
    530             535             540

Lys Trp Tyr Glu Leu Gly His Lys Arg Gly His Phe Ala Ser Val Trp
545             550             555             560

Gln Arg Ser Leu Tyr Asn Val Asn Gly Leu Lys Ala Gln Pro Trp Trp
            565             570             575

Thr Pro Lys Glu Thr Gly Tyr Thr Glu Leu Val Lys Ser Leu Glu Arg
            580             585             590

Asn Trp Lys Leu Ile Arg Asp Glu Gly Leu Ala Val Met Asp Lys Ala
        595             600             605

Lys Gly Leu Phe Leu Pro Glu Asp Glu Asn Leu Arg Glu Lys Gly Asp
    610             615             620

Trp Ser Gln Phe Thr Leu Trp Gln Gln Gly Arg Arg Asn Glu Asn Ala
625             630             635             640
```

Cys Lys Gly Ala Pro Lys Thr Cys Thr Leu Leu Glu Lys Phe Pro Glu
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Thr Thr Gly Cys Arg Arg Gly Gln Ile Lys Tyr Ser Ile Met His Pro
            660   665   670

Gly Thr His Val Trp Pro His Thr Gly Pro Thr Asn Cys Arg Leu Arg
            675   680   685

Met His Leu Gly Leu Val Ile Pro Lys Glu Gly Cys Lys Ile Arg Cys
            690   695   700

Ala Asn Glu Thr Arg Thr Trp Glu Glu Gly Lys Val Leu Ile Phe Asp
705   710   715   720

Asp Ser Phe Glu His Glu Val Trp Gln Asp Ala Ser Ser Phe Arg Leu
            725   730   735

Ile Phe Ile Val Asp Val Trp His Pro Glu Leu Thr Pro Gln Gln Arg
            740   745   750

Arg Ser Leu Pro Ala Ile
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<210> 3
<211> 2324
<212> DNA
<213> Homo sapiens

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agcatggagg acacaagaat gggaggaaag gcggactctc gggaacttca ttcttcacgt 180
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gagaaccaca acaagaggat gatgagtttc ttatggcgac tgatgtagat gatagatttg 600
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accaagtcta tgaggaacaa gcagtatatg aacctctaga aaatgaaggg atagaaatca 840
cagaagtaac tgctcccct gaggataatc ctgtagaaga ttcacaggta attgtagaag 900
aagtaagcat ttttcctgtg gaagaacagc aggaagtacc accagaaaca aatagaaaaa 960
cagatgatcc agaacaaaaa gcaaaagtta agaaaaagaa gcctaaactt ttaaataaat 1020

5

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<210> 4
<211> 31
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: EGF-like
     cysteine-rich repeat

<220>
<221> VARIANT
<222> (3)..(5)
<223> Wherein any Xaa may be any amino acid

<220>
<221> VARIANT
<222> (6)..(7)
<223> Wherein Xaa is any amino acid.

<220>
<221> VARIANT
<222> (10)
<223> Wherein Xaa is any amino acid.

6

<220>
<221> VARIANT
<222> (14)
<223> Wherein Xaa is any amino acid.

<220>
<221> VARIANT
<222> (17)..(18)

<220>
<221> VARIANT
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<223> Wherein Xaa is any amino acid.

<220>
<221> VARIANT
<222> (29)
<223> Wherein Xaa is any amino acid.

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Cys Asp Xaa Xaa Xaa Cys Xaa Xaa Lys Xaa Gly Asn Gly Xaa Cys Asp
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Xaa Xaa Cys Asn Asn Ala Ala Cys Xaa Xaa Asp Gly Xaa Asp Cys
             20   25   30

<210> 5
<211> 1242
<212> PRT
<213> Homo sapiens

<400> 5
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 1   5   10   15

Gly Tyr Leu Arg Lys Pro Lys Ser Met His Lys Arg Phe Phe Val Leu
             20   25   30

Arg Ala Ala Ser Glu Ala Gly Gly Pro Ala Arg Leu Glu Tyr Tyr Glu
         35   40   45

Asn Glu Lys Lys Trp Arg His Lys Ser Ser Ala Pro Lys Arg Ser Ile
     50   55   60

Pro Leu Glu Ser Cys Phe Asn Ile Asn Lys Arg Ala Asp Ser Lys Asn
 65   70   75   80

```
Lys His Leu Val Ala Leu Tyr Thr Arg Asp Glu His Phe Ala Ile Ala
                85                  90                  95

Ala Asp Ser Glu Ala Glu Gln Asp Ser Trp Tyr Gln Ala Leu Leu Gln
            100                 105                 110

Leu His Asn Arg Ala Lys Gly His His Asp Gly Ala Ala Ala Leu Gly
        115                 120                 125

Ala Gly Gly Gly Gly Ser Cys Ser Gly Ser Ser Gly Leu Gly Glu
    130                 135                 140

Ala Gly Glu Asp Leu Ser Tyr Gly Asp Val Pro Pro Gly Pro Ala Phe
145                 150                 155                 160

Lys Glu Val Trp Gln Val Ile Leu Lys Pro Lys Gly Leu Gly Gln Thr
                165                 170                 175

Lys Asn Leu Ile Gly Ile Tyr Arg Leu Cys Leu Thr Ser Lys Thr Ile
            180                 185                 190

Ser Phe Val Lys Leu Asn Ser Glu Ala Ala Ala Val Val Leu Gln Leu
        195                 200                 205

Met Asn Ile Arg Arg Cys Gly His Ser Glu Asn Phe Phe Phe Ile Glu
    210                 215                 220

Val Gly Arg Ser Ala Val Thr Gly Pro Gly Glu Phe Trp Met Gln Val
225                 230                 235                 240

Asp Asp Ser Val Val Ala Gln Asn Met His Glu Thr Ile Leu Glu Ala
                245                 250                 255

Met Arg Ala Met Ser Asp Glu Phe Arg Pro Arg Ser Lys Ser Gln Ser
            260                 265                 270

Ser Ser Asn Cys Ser Asn Pro Ile Ser Val Pro Leu Arg Arg His His
        275                 280                 285

Leu Asn Asn Pro Pro Pro Ser Gln Val Gly Leu Thr Arg Arg Ser Arg
    290                 295                 300

Thr Glu Ser Ile Thr Ala Thr Ser Pro Ala Ser Met Val Gly Gly Lys
305                 310                 315                 320

Pro Gly Ser Phe Arg Val Arg Ala Ser Ser Asp Gly Glu Gly Thr Met
                325                 330                 335
```

8

```
Ser Arg Pro Ala Ser Val Asp Gly Ser Pro Val Ser Pro Ser Thr Asn
        340                 345                 350

Arg Thr His Ala His Arg His Arg Gly Ser Ala Arg Leu His Pro Pro
        355                 360                 365

Leu Asn His Ser Arg Ser Ile Pro Met Pro Ala Ser Arg Cys Ser Pro
        370                 375                 380

Ser Ala Thr Ser Pro Val Ser Leu Ser Ser Ser Ser Thr Ser Gly His
385                 390                 395                 400

Gly Ser Thr Ser Asp Cys Leu Phe Pro Arg Arg Ser Ser Ala Ser Val
                405                 410                 415

Ser Gly Ser Pro Ser Asp Gly Gly Phe Ile Ser Ser Asp Glu Tyr Gly
        420                 425                 430

Ser Ser Pro Cys Asp Phe Arg Ser Ser Phe Arg Ser Val Thr Pro Asp
        435                 440                 445

Ser Leu Gly His Thr Pro Pro Ala Arg Gly Glu Glu Glu Leu Ser Asn
        450                 455                 460

Tyr Ile Cys Met Gly Gly Lys Gly Pro Ser Thr Leu Thr Ala Pro Asn
465                 470                 475                 480

Gly His Tyr Ile Leu Ser Arg Gly Gly Asn Gly His Arg Cys Thr Pro
                485                 490                 495

Gly Thr Gly Leu Gly Thr Ser Pro Ala Leu Ala Gly Asp Glu Ala Ala
        500                 505                 510

Ser Ala Ala Asp Leu Asp Asn Arg Phe Arg Lys Arg Thr His Ser Ala
        515                 520                 525

Gly Thr Ser Pro Thr Ile Thr His Gln Lys Thr Pro Ser Gln Ser Ser
        530                 535                 540

Val Ala Ser Ile Glu Glu Tyr Thr Glu Met Met Pro Ala Tyr Pro Pro
545                 550                 555                 560

Gly Gly Gly Ser Gly Gly Arg Leu Pro Gly His Arg His Ser Ala Phe
                565                 570                 575

Val Pro Thr Arg Ser Tyr Pro Glu Glu Gly Leu Glu Met His Pro Leu
                580                 585                 590
```

9

```
Glu Arg Arg Gly Gly His His Arg Pro Asp Ser Ser Thr Leu His Thr
        595                 600                 605

Asp Asp Gly Tyr Met Pro Met Ser Pro Gly Val Ala Pro Val Pro Ser
        610                 615                 620

Gly Arg Lys Gly Ser Gly Asp Tyr Met Pro Met Ser Pro Lys Ser Val
625                 630                 635                 640

Ser Ala Pro Gln Gln Ile Ile Asn Pro Ile Arg Arg His Pro Gln Arg
                645                 650                 655

Val Asp Pro Asn Gly Tyr Met Met Met Ser Pro Ser Gly Gly Cys Ser
                660                 665                 670

Pro Asp Ile Gly Gly Gly Pro Ser Ser Ser Ser Ser Ser Ser Asn Ala
                675                 680                 685

Val Pro Ser Gly Thr Ser Tyr Gly Lys Leu Trp Thr Asn Gly Val Gly
        690                 695                 700

Gly His His Ser His Val Leu Pro His Pro Lys Pro Pro Val Glu Ser
705                 710                 715                 720

Ser Gly Gly Lys Leu Leu Pro Cys Thr Gly Asp Tyr Met Asn Met Ser
                725                 730                 735

Pro Val Gly Asp Ser Asn Thr Ser Ser Pro Ser Asp Cys Tyr Tyr Gly
                740                 745                 750

Pro Glu Asp Pro Gln His Lys Pro Val Leu Ser Tyr Tyr Ser Leu Pro
        755                 760                 765

Arg Ser Phe Lys His Thr Gln Arg Pro Gly Glu Pro Glu Glu Gly Ala
        770                 775                 780

Arg His Gln His Leu Arg Leu Ser Thr Ser Ser Gly Arg Leu Leu Tyr
785                 790                 795                 800

Ala Ala Thr Ala Asp Asp Ser Ser Ser Ser Thr Ser Ser Asp Ser Leu
                805                 810                 815

Gly Gly Gly Tyr Cys Gly Ala Arg Leu Glu Pro Ser Leu Pro His Pro
                820                 825                 830

His His Gln Val Leu Gln Pro His Leu Pro Arg Lys Val Asp Thr Ala
        835                 840                 845

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Ala Gln Thr Asn Ser Arg Leu Ala Arg Pro Thr Arg Leu Ser Leu Gly
    850                 855                 860

Asp Pro Lys Ala Ser Thr Leu Pro Arg Ala Arg Glu Gln Gln Gln Gln
865                 870                 875                 880

Gln Gln Pro Leu Leu His Pro Pro Glu Pro Lys Ser Pro Gly Glu Tyr
                885                 890                 895

Val Asn Ile Glu Phe Gly Ser Asp Gln Ser Gly Tyr Leu Ser Gly Pro
                900                 905                 910

Val Ala Phe His Ser Ser Pro Ser Val Arg Cys Pro Ser Gln Leu Gln
        915                 920                 925

Pro Ala Pro Arg Glu Glu Glu Thr Gly Thr Glu Glu Tyr Met Lys Met
    930                 935                 940

Asp Leu Gly Pro Gly Arg Arg Ala Ala Trp Gln Glu Ser Thr Gly Val
945                 950                 955                 960

Glu Met Gly Arg Leu Gly Pro Ala Pro Pro Gly Ala Ala Ser Ile Cys
                965                 970                 975

Arg Pro Thr Arg Ala Val Pro Ser Ser Arg Gly Asp Tyr Met Thr Met
                980                 985                 990

Gln Met Ser Cys Pro Arg Gln Ser Tyr Val Asp Thr Ser Pro Ala Ala
        995                 1000                1005

Pro Val Ser Tyr Ala Asp Met Arg Thr Gly Ile Ala Ala Glu Glu Val
    1010                1015                1020

Ser Leu Pro Arg Ala Thr Met Ala Ala Ala Ser Ser Ser Ser Ala Ala
1025                1030                1035                1040

Ser Ala Ser Pro Thr Gly Pro Gln Gly Ala Ala Glu Leu Ala Ala His
            1045                1050                1055

Ser Ser Leu Leu Gly Gly Pro Gln Gly Pro Gly Gly Met Ser Ala Phe
        1060                1065                1070

Thr Arg Val Asn Leu Ser Pro Asn Arg Asn Gln Ser Ala Lys Val Ile
        1075                1080                1085

Arg Ala Asp Pro Gln Gly Cys Arg Arg Arg His Ser Ser Glu Thr Phe
    1090                1095                1100
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11

Ser Ser Thr Pro Ser Ala Thr Arg Val Gly Asn Thr Val Pro Phe Gly
1105   1110   1115   1120

Ala Gly Ala Ala Val Gly Gly Gly Gly Gly Ser Ser Ser Ser Ser Glu
                1125   1130   1135

Asp Val Lys Arg His Ser Ser Ala Ser Phe Glu Asn Val Trp Leu Arg
            1140   1145   1150

Pro Gly Glu Leu Gly Gly Ala Pro Lys Glu Pro Ala Lys Leu Cys Gly
            1155   1160   1165

Ala Ala Gly Gly Leu Glu Asn Gly Leu Asn Tyr Ile Asp Leu Asp Leu
    1170   1175   1180

Val Lys Asp Phe Lys Gln Cys Pro Gln Glu Cys Thr Pro Glu Pro Gln
1185   1190   1195   1200

Pro Pro Pro Pro Pro Pro Pro His Gln Pro Leu Gly Ser Gly Glu Ser
                1205   1210   1215

Ser Ser Thr Arg Arg Ser Ser Glu Asp Leu Ser Ala Tyr Ala Ser Ile
            1220   1225   1230

Ser Phe Gln Lys Gln Pro Glu Asp Arg Gln
        1235   1240

<210> 6
<211> 5828
<212> DNA
<213> Homo sapiens

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12

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13

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14

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